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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,228	07/19/2001	Anna Victoria Hine	PL-9830	7993

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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,228	HINE ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-13, 21-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-20* is/are rejected.

7)☒ Claim(s) *14-20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on June 16, 2005.

Status of the Claims

2. Claims 1-27 are pending.

3. Applicant's response to the Restriction and/or Election of Species requirements is acknowledged (Applicant elected ***with traverse*** Group III, claims 14-23) and claims 1-13 and 24-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim (see below i.e., ***Response to Restriction and/or Election of Species***).

4. Please note: Applicant's elected species (Subgroup 1 = protein libraries comprising three zinc fingers; Subgroup 2= biotinylated polynucleotide; Subgroup 4 = library of SEQ ID No. 2; Subgroup 5 = scintillation proximity assay) were found in the art. Furthermore, Applicant's *specifically* elected species (Subgroup 3 = 60 libraries grouped into three groups of 20 libraries with specified amino acids at -1 and +3 and +6 positions, respectively) was searched and was not found in the prior art. Thus, the search was expanded to non-elected species, which *were* found in the prior art, see rejections below. Also, see MPEP § 803.02 (emphasis added):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the

search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

5. Claims 21-23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, the requirement having been traversed in the 8/13/03 Response (see below i.e., ***Response to Restriction and/or Election of Species***). Although Applicants state, "... claims 14-23 read on the elected species" (e.g., see 6/16/05 Response, page 3, paragraph 2), this statement appears to be in error. Applicants' specification reads, "... Radiolabelled DNA is detected using scintillation-based methods or appropriate imaging technology. Non-radiometrically labeled DNA is detected using colorimetric techniques and a spectrophotometer" (e.g., see specification, page 37, Conclusion). Thus, a "colorimetric" technique does not read a "scintillation proximity assay" because the colorimetric technique does not employ a radiolabel and/or scintillation-based detection equipment.

6. Therefore, claims 14-20 are examined on the merits in this action.

Response to Restriction and/or Election of Species

7. Applicant's election of Group III (claims 14-23) **with traverse** is acknowledged (e.g., see 8/13/03 Response, page 12, last paragraph).

8. The traversal is on the ground(s) that **[1]** "... all the groups of the invention do relate to a single inventive concept under PCT Rule 13.1. Indeed, Applicants respectfully point out to the Examiner that the IPEA clearly did not arrive at the same position as the Examiner regarding the unity of an invention" (e.g., see 8/13/03 Response, page 13, paragraph 1; see also page 14, paragraph 1), **[2]** "Contrary to what the Examiner has said, Applicants respectfully submit that the claims within Group I claim a set of libraries, which codes for proteins capable of specific binding interactions, which are the same proteins that are claimed in claims 7-12" (e.g., see 8/13/03 Response, page 13, paragraph 1), **[3]** "Group III, claims 14-23, uses the set of protein libraries defined in claim 7, which clearly links this group to the previous group [i.e., Group II]" (e.g., see 8/13/03 Response, page 13, paragraph 2), **[4]** "Group IV (claim 24), is avariant of the broader generic sequence recited in claim 6 and Group V is a gene which codes for this protein. As such these two groups are connected back to the original group by the common inventive concept (e.g., see 8/13/03 Response, page 13, paragraph 2) and **[5]** "Finally, the method for constructing randomized gene libraries of Group VI is a method for producing randomized gene libraries as recited in previous claims. As such, Applicants respectfully submit that this is linked by the same inventive entity to the other groups" (e.g., see 8/13/03 Response, page 13, last paragraph).

9. These arguments were fully considered but were not found persuasive. **[1]** The Examiner maintains that Groups I-VI do not relate to a single inventive concept for the reasons outlined in the 7/11/03 Restriction requirement (e.g., see 7/11/03 Restriction, paragraphs 1-16, which are incorporated in their entirety herein by reference). Furthermore, it should be noted that the PTO

is not bound by the IPEA decisions and did not have the same references before (i.e., the IPEA did not consider the PNAS reference by Choo et al. when it made its decision). **[2]** The Examiner respectfully disagrees. Group I is drawn to a library of genes (e.g., DNA) whereas Group II is drawn to a library of proteins. These molecules do not share any structural features whether one codes for the other or not. Furthermore, the "genes" contain sequences (e.g., introns, promoter regions, etc.) that do not encode for said proteins. In addition, even if *assuming arguendo* that said genes did share a common feature with the proteins in claims 7-12, the shared technical feature would not constitute a special technical feature because this feature is known in the art (e.g., see 7/11/03 Restriction Requirement; see also 35 U.S.C. § 102 rejection below). **[3]** The linkage to which Applicants refer does not constitute a special technical feature because this feature is known in the art as demonstrated by the Choo et al. reference (e.g., see 7/13/03 Restriction, see also 35 U.S.C. § 102 rejection below). **[4]** As stated in the original restriction (e.g., see 7/13/03 Restriction, page 3, paragraph 6, "Groups I ... IV and V do not share a technical feature because they represent distinct products. For example, Groups I and V are drawn to "gene products whereas Group ... IV [is] drawn to 'protein' products. Each nucleic acid is structurally and functionally distinct from each polypeptide. Likewise, Groups I ... are drawn to a 'library' whereas Groups IV and V are not. The libraries of Groups I ... would not necessarily contain the individual members of Groups IV and V"), Groups I, IV and V do not share a special technical feature. The library of Group I would not "necessarily" contain members of Groups IV and V and thus these Groups are not necessarily related in any way. **[5]** Group VI does not share a special technical feature with the previous claims. For example, Groups II and IV are not linked because they are drawn to different methods that use different

method steps and/or reagents. Group II requires "proteins" for binding partner "screening" whereas Group IV requires "nucleic acids" for the production of a "gene library". Likewise, Group VI requires making gene libraries that would not necessarily contain the gene product of Group V, nor would it necessarily result in the protein products of Groups II and V because Group II does not require a "fully" randomized library and the sequence disclosed in Group V would not necessarily be encoded by Applicants' claimed gene library. Consequently, Group VI is properly restricted as set forth in the original restriction (e.g., see 7/13/03 Restriction, paragraphs 1-16, which is incorporated in its entirety herein by reference).

10. Applicant's election of species with traverse is also acknowledged.

11. The election of species traversal [with regard to Subgroup 2 only] is on the ground(s) that "... the degree of biotinylation of the polynucleotide is not at issue in the claim. Indeed as defined at claim 9, lines 18-20, the term 'polynucleotide' is something which Applicants respectfully assert is well understood" (e.g., see 8/13/03 Response, page 15)..

12. These arguments were fully considered but were not found persuasive. The examiner's position is that the species are distinct, each from the other, for the reasons stated of record (e.g., see 7/11/03 Restriction, paragraphs 17-25, which are incorporated in their entirety herein by reference). In addition, PCT Rule 13.2 states that unity of invention shall be fulfilled when ... (a) all alternatives have a common property; and (b)(i) a common structure is present ..." (e.g., see 7/11/03 Restriction, paragraph 24). Here, the a polynucleotide and a biotinylated

polynucleotide share a common structure (i.e., polynucleotide), but do not have a common property (e.g., the non-biotinylated polynucleotide does not bind to streptavidin). Thus, they do not share a special technical feature. Furthermore, the nucleic acid is "known in the art" and thus cannot constitute a special technical feature (e.g., see 7/13/03 Restriction, paragraph 10; see also 35 U.S.C. § 102(b) rejection below).

13. Applicant's election of species in the 8/13/03 [i.e., with respect to Subgroups 1 and 5] and 2/9/05 [i.e., with respect to Subgroups 3 and 4] responses is also acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of species has also been treated as an election without traverse (MPEP § 818.03(a) and/ or 37 CFR 1.111(b)). In the 2/9/5 Response, Applicants stated that the "traversal" was on the same grounds as that provided n the 8/13/03 Response. However, no such traversal with respect to Subgroups 3 and 4 was set forth in the 8/13/03 Response. Only and alleged error in Subgroup 2 was "distinctly and specifically" pointed to in the 8/13/03 Response.

14. As a result, the restriction requirement and/or election of species is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

15. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless

the references have been cited by the examiner on the form PTO-892, they have not been considered.

Specification

16. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). Here, reference to PCT/GB99/03081 (filed 9/14/1999) is missing from the first sentence in the specification.

17. The disclosure is further objected to for omitting the "Brief Description of the Several Views of the Drawing(s)." See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR § 1.74 is required. No new matter should be added upon amendment.

Objections to the Claims

18. Claims 14-20 are objected to because of the following informalities:

A. This application contains "hybrid" claims that are based in part on a nonelected invention (e.g., claim 14 is "dependent" on non-elected claim 7). See MPEP § 821. The Examiner recommends amending claim 14 to incorporate the limitations of non-elected claim 7 into claim 14.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 14-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claim 14**, the phrase "providing a set of libraries of proteins as defined in claim 7" is vague and indefinite because the limitations of claim 7 that are incorporated by reference into claim 14 are vague and indefinite. For example, claim 7 discloses, "6 to 20 libraries in each of which libraries said first specified position is randomized and a different amino acid is present at at least one other specified position" in step b) of the claim. However, there is no point of reference to ascertain whether an amino acid is "different" or not at the at least one other specified position. Does the amino acid at the at least one other specified position have to be different from the randomized position? Does the amino acid at the at least one other specified position have to be different from an amino acid at the at least one other specified position from one of the other members of the 6 to 20 libraries. There is simply no point of reference. Applicants are requested to clarify and/or correct. Therefore, claims 14 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 14-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Choo et al. (WO 96/06166) (Date of Patent is **February 29, 1996**).

For ***claim 14***, Choo et al. (see entire document) disclose "libraries of DNA sequences encoding zinc finger binding motifs for display on a particle [e.g., phage], together with methods of ... use ... for various *in vitro* or *in vivo* applications" (e.g., see Choo et al., abstract), which anticipates the claimed invention. For example, Choo et al. disclose a method of identifying a protein that interacts with a specific binding partner (e.g., see figure 4 wherein the "specific binding partners" represent members of the 12 oligonucleotide libraries i.e., GNN, ANN, TNN, etc. and the "proteins that interact with the specific binding members" include the α-helix sequences shown i.e., RSDHLTTHIR, RYDALEAHRR, etc. that are subsequently "identified" by their binding signatures). Choo et al. also disclose providing a set of libraries of proteins as defined in claim 7. For example, Choo et al. disclose **(a)** 6 to 20 libraries in which each library has at least one but less than 20 amino acid residues at the said first specified position and is randomized at the said at least one other determined position (e.g., see figure 4, α-helix sequence entries wherein Library 1a = RSDHLTTHIR + RVDALEAHRR, Library 2a = RLDGLRTHLK + RADALMVHKR, Library 3a = RSDTLKKHGK + RGDALTSHER, Library 4a = RGDHLKDHIK + RGPDLARHGR, Library 5a = REDVLIRHGK + RSDLLQRHHK, Library 6a = RQDTLVGHER + RAADLNRHVR, 7a = RKDVLVSHVR + RRDVLMNHIR, etc.; please note that many other interpretations are

possible). In libraries 1a-7a above, each library has at least one but less than 20 amino acid residues at the said first specified position (i.e., each library has an "R" at the first specified "-1" position; see also paragraph bridging pages 26-27 showing positions -1, +3 and +6 are "involved in the recognition [i.e., capable of specific binding interactions] of DNA"; see also Discussion describing the importance of the -1, +3 and +6 positions in DNA recognition). In addition, libraries 1a-7a above contain an at least one other determined position that is randomized (e.g., see figure 2 showing "randomized" positions at 1, 2, 3, 5, 6 and 8 marked with an "X"; see also figure 4 showing, for example, random incorporation of "S" and "V" at position 1 in Library 1 = RSDHLTTHIR + RVDALEAHRR; see also page 5, lines 3-4, "the sequences coding for zinc finger binding motifs having random allocation of amino acids at positions -1, +2, +3, +6 and at least one of positions +1, +5 and +8"). Furthermore, libraries 1a-7a are arranged in such a way that a specific binding partner identifies an amino acid residue at the said first specified position that takes part in the specific binding interaction (e.g., see figure 4, right hand side wherein the "binding site signatures" are disclosed that results from a unique "arrangement" of the libraries with respect to the twelve target oligonucleotide libraries; see also, for example, entries listed 4 and 6 from the bottom of figure 4 that begin with "RRD ..." and "SRD ..." showing that a one amino acid change, R → S at position -1, is responsible for a change in binding affinity to the TNN target i.e., R at position -1 is "identified" as a strong binder and S at position -1 is "identified" as a weak binder with respect to the TNN target). In addition, Choo et al. disclose **(b)** 6 to 20 libraries in each of which libraries said first specified position is randomized and a

different amino acid is present at least one other specified position (e.g., see figure 4 entries wherein Library 1b = **N**RDTLT**R**HSK + **T**PGNLT**R**HGR; Library 2b = **N**GGNLG**R**HMK + **N**QSNLE**R**HHR; Library 3b = **D**RSNLE**R**HTR + **Q**QSNLV**R**HQR; Library 4b = **N**GANLE**R**HRR + **S**QGNLQ**R**HGR; Library 5b = **T**GGSLARHER + **D**HANLARHTR; Library 6b = **L**QSNLVRHQR + **Q**GGNLV**R**HLR; Library 7b = SRDVLR**R**HNR + **E**KATLA**R**HMK; please note that many other interpretations are possible). In this scenario, the library positions at the "-1" position are randomized (e.g., see "bolded" amino acids above; see also page 5, lines 3-4, "the sequences coding for zinc finger binding motifs having random allocation of amino acids at positions -1"). Furthermore, all of the amino acids located at the +6 position (i.e., the "at least one other specified" position) are "different" than the amino acids at the -1 position (e.g., compare amino acids at "underlined" +6 positions, which are all "R" groups, to the "bolded" amino acids at the -1 position i.e., N, T, etc.). Choo et al. also disclose incubating the specific binding partner with each library of the set and observing specific binding interactions with certain libraries of the set (e.g., see figure 4 wherein the intensity of the "shaded" boxes indicates "observed specific binding interactions" for each library member). Finally, Choo et al. disclose using the observations to identify a protein which interacts with the specific binding pattern (e.g., see figure 4, right hand side wherein the "binding site signatures" are disclosed; see also, for example, entries 4 and 6 from the bottom that begin with "RRD ..." and "SRD ..." showing that a one amino acid change, R → S at position -1, is responsible for a change in binding affinity to the TNN target i.e., R at position -1 is "identified" as a strong binder and S at position -1 is "identified" as a

weak binder with respect to the TNN target).

For ***claim 15***, Choo et al. disclose polynucleotides (e.g., see figure 4 wherein GNN, ANN, etc. are disclosed).

For ***claim 16***, Choo et al. disclose radiometric and luminescent assays (e.g., see figure 10; see also page 14, second to last paragraph, "Modification of the nucleic acid of interest (in the sense of binding thereto by a zinc finger polypeptide) could be detected in any of a number of methods (e.g., gel mobility shift assays, use of labeled zinc finger polypeptides – labels could include radioactive, fluorescent, enzyme or biotin/streptavidin labels"; see also figure 11).

For ***claim 17***, Choo et al. disclose "imaging" (e.g., see figure 10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claims 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choo et al. (WO 96/06166) (Date of Patent is **February 29, 1996**) and Udenfriend et al. (Udenfriend, S.; Gerber, L.; Nelson, N. "Scintillation Proximity Assay: A Sensitive and Continous Isotopic Method for Monitoring Ligand/Receptor and Antigen/Antibody Intereactions" *Anal. Biochem.* **1987**, *161*, 494-500).

For ***claims 14-17***, Choo et al. teach all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 14-17.

The prior art teaching of Choo et al. differ from the claimed invention as follows:

For ***claim 18-20***, the prior art teachings of Choo et al. differ from the claimed invention by not specifically reciting the use of a scintillation proximity assay. Choo et al. only teach the use of radiolabels in general, but not specifically refer to the SPA technique (e.g., see Choo et al., page 14, second to last paragraph, "Modification of the nucleic acid of interest (in the sense of binding thereto by a zinc finger polypeptide) could be detected in any of a number of methods (e.g., gel mobility shift assays, use of labeled zinc finger polypeptides – labels could include radioactive, fluorescent, enzyme or biotin/streptavidin labels)").

However, Udenfriend et al. teach the following limitations that are deficient in Choo et al.:

For ***claim 18***, Udenfriend et al. (see entire document) teach the use of a scintillation proximity assay (e.g., see Udenfriend et al., abstract).

For ***claim 19***, Udenfriend et al. teach the use of radiolabeled binding partners and immobilized proteins (e.g., see figures 1 and 2 wherein proteins are immobilized on bead surface that subsequently react with radiolabeled binding partners; see also abstract).

For ***claim 20***, Udenfriend et al. disclose the use of a washing step (e.g., see figure 4 wherein the ^{125}I-labeled heptapeptide is displaced (i.e., washed) from the anti-heptapeptide Ab beads; see also figure 6 wherein the labeled agonist is washed from the beads using higher affinity agonists in a competition experiment).

It would have been *prima facie* obvious to one skilled in the art at the time the invention was made to use the "scintillation proximity assay" as taught by Udenfriend et al. to detect the zinc finger/DNA interactions as taught by Choo et al. because Udenfriend et al. explicitly state that their assay can be used for monitoring ligand/receptor interactions including protein/DNA interactions (e.g., see Choo et al., abstract), which would encompass the zinc finger protein/ DNA ligand interactions disclosed by Choo et al. (e.g., see Choo et al., figure 4). Furthermore, one of ordinary skill in the art would have been motivated to use the Scintillation Proximity Assay because Udenfriend et al. explicitly state, "Scintillation proximity assay (SPA) makes it possible to use radioisotopes for monitoring binding reactions continuously without the need to separate free from bound components. As a result SPA can be carried out more rapidly than most other methods ... The method also lends itself to automation ... Another feature of SPA is that the key reagents ... are relatively inexpensive" (e.g., see Choo et al., abstract; see

also page 495, column 1, paragraph 1, "The methodology is rapid, simple, and sensitive and, what is most important, permits kinetic measurements under steady-state conditions"). Finally, one of ordinary skill in the art would have reasonably expected to be successful because Udenfriend et al. state that both proteins and nucleic acids can be used in a scintillation proximity assay (e.g., see Udenfriend et al., abstract; see also page 499, paragraph 3, "The few applications of SPA reported above do not represent all that can be done with this system ... [SPA] can be used to monitor almost any reaction"), which would encompass the zinc finger protein/DNA interactions disclosed by Choo et al. (e.g., see Choo et al., figure 4). In addition, Udenfriend et al. state, "[t]he sensitivities already achieved with SPA procedures are comparable to the sensitivities of other procedures in use today" (e.g., see Udenfriend et al., abstract). Further Choo et al. state that radioisotopes, like the ones disclosed by Udenfriend et al. (e.g., see Udenfriend et al., abstract), are compatible with their method (e.g., see Choo et al., page 14, second to last paragraph).

References Illustrative of the State of Prior Art

23. Applicants' elected species SEQ ID NO: 2 is known in the art as exemplified by Krizek et al. (Krizek, B. A.; Zawadzke, L. E.; Berg, J. M. "Independence of metal Binding between tandem Cys2His2 zinc finger domains" *Protein Science* **1993**, *2*, 1313-1319, see especially figure 2, entry CP-CP).

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The

examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
September 12, 2005